UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY
CAMDEN VICINAGE

IN RE: VALSARTAN, LOSARTAN, AND IRBESARTAN PRODUCTS LIABILITY LITIGATION **THIS DOCUMENT RELATES TO:** *Gaston Roberts et al. v. Zhejiang Huahai Pharmaceutical Co., et al.*, Case No. 1:20-cv-00946-RBK-JS	MDL No. 2875 Honorable Renée Marie Bumb District Court Judge

DEFENDANTS' MEMORANDUM IN SUPPORT OF MOTION TO EXCLUDE THE OPINIONS OF DR. WILLIAM SAWYER

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INTRODUCTION

Dr. William Sawyer, a professional expert, seeks to testify at trial that valsartan containing NDMA ("valsartan") can cause liver cancer, relying in part on dietary studies, in part on literature involving rubber factory workers, and in part on fabricated citations. Dr. Sawyer's unreliable and speculative opinions fall far short of the requirements of Rule 702.

First, Dr. Sawyer cites to, and relies upon, numerous falsified sources that likely resulted from his use of artificial intelligence ("AI") to draft his expert report. Dr. Sawyer then lied at his deposition, claiming that he had actually read the non-existent articles and that the questioner was mistaken in doubting their existence. Dr. Sawyer's use of falsified sources in formulating his opinions and his dishonesty during his deposition "shatter" his reliability as an expert and independently warrant wholesale exclusion of his expert opinions. *See Kohls v. Ellison*, No. 24-CV-3754 (LMP/DLM), 2025 WL 66514, at *3 (D. Minn. Jan. 10, 2025) (excluding expert who "admit[ted] that he used GPT-4o to assist him in drafting his declaration but . . . failed to discern that [it] generated fake citations to academic articles").

Second, Dr. Sawyer equivocated on whether he is offering a general causation opinion, vaguely suggesting that he intends to rely on the general causation opinions previously offered in this MDL proceeding. To the extent he has retracted his general causation opinion, it should be excluded from trial on that basis alone. To the extent

Dr. Sawyer still intends to testify on causation, however, his opinion is not the product of any discernible—much less reliable—methodology. As an initial matter, he relies heavily on animal, dietary and occupational studies that the *Zantac* MDL court recognized cannot support a causal opinion regarding what (if any) relationship exists between exposure to NDMA in medication and cancer in humans. *See In re Zantac (Ranitidine) Prods. Liab. Litig.*, 644 F. Supp. 3d 1075 (S.D. Fla. 2022). This is doubly true because many of those studies do not even involve liver cancer, and it is basic science that an expert cannot determine that an exposure causes one type of cancer based on studies involving a different cancer.

In addition, Dr. Sawyer's Bradford Hill analysis is superficial, misapplies the applicable criteria and is results-driven. For example, although Dr. Sawyer states in his report that there is "no debate" that the strength of the association is "potent" (Sawyer Rep. at 79 (Ex. 1 to Decl. of Nina Rose ("Rose Decl.")), he was unable to defend that claim at his deposition, ultimately conceding that the 1.12 and 1.16 relative risks reported in the only two epidemiological studies that found a statistically significant association between valsartan use and liver cancer (Mansouri 2022 and Gomm 2021, respectively) are "weak." Dr. Sawyer also claims that consistency is satisfied by relying on a fake article that does not exist. And Dr. Sawyer states in his report that the literature supports a dose-response relationship (i.e., risk increased with amount of exposure), but that is simply not true; in fact,

Mansouri 2022 found an ***inverse*** relationship between dose and disease. Dr. Sawyer's claim of coherence similarly ignores numerous anomalies in the NDMA-valsartan epidemiology that render Dr. Sawyer's causation opinion incoherent with scientific knowledge. And his opinion is also at odds with the near-universal recognition by scientists that liver cancer has a much longer latency period than the less-than-two-year period Plaintiff alleges it took Mr. Roberts to develop this disease.

Finally, Dr. Sawyer purported to perform a dose extrapolation exercise to compare the amount of NDMA that may have been inhaled by rubber factory workers in a 2019 occupational exposure study (Hidajat 2019) to the amount of NDMA that Mr. Roberts may have orally ingested from valsartan because the rubber workers in that study were found to have an increased risk of liver cancer. (*See* Sawyer Rep. at 52-62, 74-77.) But Dr. Sawyer's dose extrapolation calculations utilize a methodology that Dr. Sawyer admits has never been scientifically validated (he essentially made it up out of thin air) and is, in any event, based on data from Hidajat 2019 that have been recognized as unreliable by the *Zantac* court.

As this Court recently recognized, Rule 702 was "amended to clarify the rigorous and essential gatekeeping function that is required of district courts." *In re Valsartan, Losartan, & Irbesartan Prods. Liab. Litig.*, MDL No. 19-2875 (RMB/SAK), 2025 U.S. Dist. LEXIS 66185, at *39 (D.N.J. Apr. 7, 2025) (Bumb,

J.). Particularly in light of that clarification, "it is not for the courts to be the pioneers, forging new trails in scientific thinking, especially when that means departing from well-established research principles[.]" *In re Acetaminophen - ASD-ADHD Prods. Liab. Litig.*, 707 F. Supp. 3d 309, 362 (S.D.N.Y. 2023) (citation omitted). Because admitting Dr. Sawyer's opinions, which rely on non-existent literature and defy basic scientific principles, would do precisely that, the Court should exclude them under Rule 702.

BACKGROUND

A. NDMA Epidemiology

Three peer-reviewed, published studies have evaluated whether there is an association between the use of valsartan containing NDMA and the development of cancer. Of these three studies, two reported weak associations between use of valsartan with NDMA and liver cancer. Below are brief summaries of the studies.

Pottegard 2018[1] examined 5,150 Danish patients who used valsartan containing NDMA for a median of 4.6 years. There was no statistically significant elevated overall risk of cancer (HR 1.09 (CI 95%: 0.85-1.41)) among valsartan users, and no liver cancers occurred in individuals exposed to valsartan containing

[1] Pottegard, Anton, et al., Use of N-nitrosodimethylamine (NDMA) Contaminated Valsartan Products and Risk of Cancer: Danish Nationwide Cohort Study. *BMJ*. 2018; 362:1-7 ("Pottegard 2018") (Rose Decl. Ex. 2).

NDMA.[2] The authors also found "no evidence of a dose-response relation" between valsartan use and development of cancer generally, noting that the group with the highest cumulative exposure to NDMA-containing valsartan had a lower hazard ratio (HR 1.11 (95% CI: 0.82-1.50)) than those with the lowest cumulative exposure to NDMA-containing valsartan (HR 1.15 (95% CI: 0.83-1.59)).[3]

Gomm 2021[4] included 780,871 individuals over 40 years old who filled a prescription for valsartan between 2012 and 2017. The study authors detected "a slight elevation in the risk of liver cancer with the use of potentially NDMA-contaminated valsartan" (HR 1.16 (95% CI: 1.03-1.31)), but a sub-analysis of "long-term valsartan use" did not find a statistically significant association with liver cancer (HR 1.22 (95% CI: 0.80-1.89)).[5] The data also showed no dose-response relationship between valsartan containing NDMA and liver cancer.[6] The authors stated that "the present study can only state the existence of a statistical association"

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2 *Id.* at 6.

3 *Id.* at 1, 5 Table 2.

4 Gomm, Willy, et al., N-Nitrosodimethylamine- Contaminated Valsartan and the Risk of Cancer. *Medicine*. 2021; 118:357-62 ("Gomm 2021") (Rose Decl. Ex. 3).

5 *Id.*

6 *Id.* ("no dose-dependent effect on the risk of liver cancer was found for higher exposure to potentially NDMA-contaminated valsartan"); *see also id.* at 360 Table 2 (noting HR of 1.15 for the lowest category of dose and HR of 1.13 for the highest category of dose among individuals diagnosed with liver cancer).

and "[c]ausality cannot be inferred" from the study's results.[7] The authors noted that they were unable to rule out residual confounding, and this paper included numerous types of liver cancer beyond HCC, the most common liver cancer and the one with which Mr. Roberts was diagnosed.

Mansouri 2022[8] studied 1.4 million people from a national database of French residents, almost 1 million of whom were considered exposed to valsartan containing NDMA. The Mansouri 2022 authors found "a slight increased risk of liver cancer . . . in patients exposed to NDMA in regularly taken medications" (HR 1.12 (95% CI: 1.04-1.22)).[9] Oddly, the study found a protective effect from use of valsartan containing NDMA and liver cancer in women (HR 0.90 (95% CI: 0.75-1.07)). In addition, the increased risk was limited to the poorest 20% of participants (social deprivation index quartile 5), suggesting that the study may have been affected by confounding.[10] Like the other studies, the authors "found no evidence of a dose–response relationship between the daily dose of valsartan and the risk of any cancer by location."[11] In fact, the hazard ratios for liver cancer were higher in

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7 *Id.* at 360.

8 Mansouri, Imene, et al. N-nitrosodimethylamine-Contaminated Valsartan and Risk of Cancer: A Nationwide Study of 1.4 Million Valsartan Users. *J. of the Am. Heart Ass'n*. 2022; 11:1-13 ("Mansouri 2022") (Rose Decl. Ex. 4).

9 *Id* at 10 fig. 3.

10 *Id.*

11 *Id* at 9.

patients with lower doses.[12] The authors concluded that "[m]ore research is needed" to "establish clinically relevant causality."[13]

B. Dr. Sawyer's Proffered Expert Opinions

Dr. Sawyer's report includes a full causal analysis under the Bradford Hill framework, although he was confused at his deposition as to whether or not he is offering a general causation opinion. Regarding strength, Dr. Sawyer concludes that there is "little or no debate that NDMA is a potent probable human carcinogen." (Sawyer Rep. at 79.) Dr. Sawyer also states that the human epidemiological evidence is "reasonabl[y] consisten[t]" in showing an association with liver cancer, although he admits "[d]ietary studies were less consistent." (*Id.*) Dr. Sawyer also opines that "[m]any of the studies revealed statistically significant dose-response effects" and *in vitro* and animal studies demonstrate the plausibility, coherence, and experiment considerations have been met. (*See id.* at 79-80.) He offers a circular opinion with respect to temporality, and he argues that NDEA, another nitrosamine compound not at issue, is also associated with cancer, which he claims fulfills the analogy consideration. (*See id.* at 80.)

Dr. Sawyer also purports to convert the inhaled NDMA exposures observed

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12 *Id.* (HR 1.14 (95% CI: 1.02-1.27) in patients treated with 80 mg/day or less and 0.99 (95% CI: 0.71-1.37) in patients treated with more than 160mg/day).

13 *Id.*

in the Hidajat 2019 study—which the *Zantac* court described as involving a "staggering" number of assumptions and estimations, *see* 644 F. Supp. 3d at 1215—to an amount of NDMA that would be orally ingested (*see generally* Sawyer Rep. at 52-62). Dr. Sawyer's proposed extrapolation method has not been peer-reviewed or published in its entirety in any scientific source. (Sawyer 5/2/2025 Dep. 19:16-20:10 (Rose Decl. Ex. 5); *see also id.* 17:6-13; 18:6-22.)

ARGUMENT

Under recently-amended Fed. R. Evid. 702, plaintiffs have the burden of "demonstrat[ing] to the court that it is more likely than not" that their expert is sufficiently qualified to offer his proposed testimony; that the expert's opinions are "based on sufficient facts or data"; that the opinions are the "product of reliable principles and methods"; and that they reflect a "reliable application of the principles and methods to the facts of the case." Fed. R. Evid. 702. As this Court recently recognized, the recent amendments were "'made necessary by the courts that have failed to apply correctly the reliability requirements of'" Rule 702. *In re Valsartan*, 2025 U.S. Dist. LEXIS 66185, at *39 (citing Fed. R. Evid. 702, advisory committee's note to 2023 amendments). In addition, "[t]he Third Circuit has also recently reemphasized the district court's 'rigorous gatekeeping function.'" *Id.* at *40 (citing *Cohen v. Cohen*, 125 F.4th 454, 460-61, 463 (3d Cir. 2025)) ("[t]he District Court's process fell short of the rigor required by . . . Rule 702" by admitting

evidence "unsupported by 'good grounds'" and reliant on inapposite studies). In short, "[t]he Court is required to analyze the expert's data and methodology at the admissibility stage more critically than in the past." *Boyer v. City of Simi Valley*, No. 2:19-cv-00560-DSF-JPR, 2024 U.S. Dist. LEXIS 44185, at *3 (C.D. Cal. Feb. 13, 2024).[14] The Court should exclude Dr. Sawyer's opinions under this standard for multiple reasons.

I. DR. SAWYER'S USE OF FALSIFIED CITATIONS WAS NOT A RELIABLE METHODOLOGY, SOUGHT TO DECEIVE THE COURT, AND SHATTERED HIS CREDIBILITY.

In formulating his opinions in this case, Dr. Sawyer relied on numerous fabricated, non-existent, and possibly AI-generated scientific articles, and then falsely testified that he had actually reviewed and considered these fake sources.

Courts "do not, and should not, 'make allowances for a [party] who cites to

[14] *See also, e.g., In re Onglyza (Saxagliptin) & Kombiglyze (Saxagliptin & Metformin) Prods. Liab. Litig.*, 93 F.4th 339, 348 n.7 (6th Cir. 2024) ("Rule 702's recent amendments . . . were drafted to correct some court decisions incorrectly holding 'that the critical questions of the sufficiency of an expert's basis . . . are questions of weight and not admissibility.'") (citation omitted); *Sardis v. Overhead Door Corp.*, 10 F.4th 268, 283-84 (4th Cir. 2021) (amendments to Rule 702 were adopted "to address this 'pervasive problem'" of "holding" that an expert's reliance on insufficient data and misapplication of principles and methods "were ones of weight for the jury") (citation omitted); *In re Acetaminophen*, 707 F. Supp. 3d at 334-35 & n.27 ("[O]ne purpose of the amendment was to emphasize that '[j]udicial gatekeeping is essential . . . .'") (citation omitted); *Optical Sols., Inc. v. Nanometrics, Inc.*, No. 18-cv-00417-BLF, 2023 U.S. Dist. LEXIS 208824, at *4-5 (N.D. Cal. Nov. 21, 2023) (expert evidence did not satisfy prior version of Rule 702, "let alone . . . the more stringent standard under the amendment to Rule 702").

fake, nonexistent, misleading authorities[.]'" *Kohls*, 2025 WL 66514, at *5 (citation omitted); *see also Dukuray v. Experian Info. Sols.*, No. 23 Civ. 9043 (AT) (GS), 2024 WL 3812259, at *11 (S.D.N.Y. July 26, 2024) ("[A]n attempt to persuade a court or oppose an adversary by relying on 'non-existent precedent generated by ChatGPT' is an 'abuse of the adversary system.'") (citation omitted).

In *Kohls*, for example, the proposed expert submitted a declaration that "included citations to two non-existent academic articles and incorrectly cited the authors of a third article." *Kohls*, 2025 WL 66514, at *3. The expert "admit[ted] that he used GPT-4o to assist him in drafting his declaration, but, in reviewing the declaration, failed to discern that GPT-4o generated fake citations to academic articles." *Id.* Although the expert provided a "detailed explanation of his drafting process to explain precisely how and why these AI-hallucinated citations in his declaration came to be" and "assure[d] the Court that he st[ood] by the substantive propositions in his declaration, even those that are supported by fake citations," the Court excluded the report on the basis that the expert's "citation to fake, AI-generated sources in his declaration . . . shatter[ed] his credibility with this Court" and "undermine[d] the expert's competence and credibility[.]" *Id.* at *4-5. The court further explained that "when attorneys and experts abdicate their independent judgment and critical thinking skills in favor of ready-made, AI-generated answers, the quality of our legal profession and the Court's decisional process suffer." *Id.* at

*4.

Dr. Sawyer committed even more egregious methodological errors in this case. Dr. Sawyer admitted that his report contains numerous falsified citations that he used to support his expert opinions in this case. (Sawyer 5/2/2025 Dep. 72:13-17 ("Q. Dr. Sawyer, there are a number of citations in your report that do not appear to be to articles that exist. Is that right? . . . . [A.] It appears that way, yes.").) Defense counsel located multiple footnotes that cited non-existent scientific articles.[15] Dr. Sawyer ultimately admitted that the falsified studies resulted from either Google or AI, which Dr. Sawyer used to locate studies (*id.* 73:2-11), and that he used "wording [taken] directly" from them in drafting sections of his report (*id.* 73:17-20, 67:22-68:3, 74:17-19).

Far from providing any "detailed explanation of his drafting process to explain precisely how and why these AI-hallucinated citations in his declaration came to be," *Kohls*, 2025 WL 66514, at *3-4, Dr. Sawyer repeatedly and falsely testified at his deposition both that these phantom articles ***do*** exist ***and*** that he had actually reviewed them. (*See* Sawyer 5/2/2025 Dep. 63:14-25 (asserting that Yuan 2027 "is a real article that [he] reviewed"); *see also id.* 70:12-71:7 ("I recall reviewing

[15] (*See, e.g.*, *id.* 45:6-9, 52:15-53:7 (footnote 5); *id.* 53:19-54:5, 54:20-57:10, 57:24-58:20, 59:5-14 (footnote 3); *id.* 60:13-23, 62:22-63:16 (footnote 4); *id.* 64:14-22, 65:6-16, 67:10-12 (footnote 6); *id.* 68:9-17, 69:4-16 (footnote 7); *id.* 70:8-22, 71:1-25 (footnote 107).)

[Sokolow paper], and I included the link . . . which was functional.").)

The fake citations are not inadvertent or trivial errors; nor are they merely background information or peripheral aspects of Dr. Sawyer's report that can be sorted out through cross-examination. Rather, they go to the heart of Dr. Sawyer's opinions (i.e., his proffered "basis"). *See In re Valsartan*, 2025 U.S. Dist. LEXIS 66185, at *23 (Rule 702 requires courts to scrutinize the "basis" for the opinion). For example, in opining on the potential mechanisms by which NDMA can allegedly cause liver cancer (*see generally* Sawyer Rep. at 6), Dr. Sawyer relies on a non-existent article published in the non-existent Journal of Hepatic Research, which he testified was a "good journal" and "sufficiently reliable" to be included in his expert report. (Sawyer 5/2/2025 Dep. 45:6-22, 46:12-18; *see also id.* 46:22-24, 47:7-48:1.) Similarly, Dr. Sawyer relies on a non-existent article as support for his claim that the studies addressing NDMA and liver cancer are consistent. (*Id.* 70:8-71:25.)[16]

For this reason alone, the Court should exclude all of Dr. Sawyer's opinions.

[16] While Plaintiff's counsel located a completely different article that Dr. Sawyer purportedly "meant to refer to" in his report to support his consistency opinion (Sawyer 5/2/2025 Dep. 134:3-5), that citation has nothing to do with consistency of association between valsartan containing NDMA and liver cancer, but rather concluded that there was no association between the intake of red meat and bladder cancer (*id.* 156:23-157:16).

II. DR. SAWYER'S GENERAL CAUSATION OPINION IS UNRELIABLE.

Despite devoting a portion of his report to the Bradford Hill framework (a methodology employed by epidemiologists to assess whether an exposure causes a disease), Dr. Sawyer repeatedly testified that he does not know if he is providing a general causation opinion in this case. (Sawyer 5/1/2025 Dep. 54:2-9 (Rose Decl. Ex. 6); *id.* 101:15-21.) This appears to be a recurring practice with Dr. Sawyer, who has previously equivocated on whether he is offering real general causation opinions in other mass tort litigation. *See In re Roundup Prods. Liab. Litig.*, No. 16-md-02741-VC, Amended Pretrial Order No. 201 (N.D. Cal. Jan. 22, 2020), ECF No. 9142 (Rose Decl. Ex. 7) (noting that "[t]he bulk of Monsanto's motions to exclude testimony from Sawyer is moot, because the plaintiffs have clarified that Sawyer does not intend to offer . . . an opinion on general causation"). If Dr. Sawyer is not actually opining on general causation, then all of his opinions on this subject should be excluded because he has retracted them. *See, e.g.*, *Wilhelm v. Ameristep Corp.*, No. 7:15-CV-00362, 2018 WL 6272911, at *22 (W.D. Va. Nov. 30, 2018) ("[W]here an expert testified that he had no opinion about a specific subject, he may not offer any opinions on that subject."); *Am. S.S. Co. v. Hallett Dock Co.*, No. CIV. 09-2628 (MJD/LIB), 2013 WL 308907, at *3 (D. Minn. Jan. 25, 2013) (excluding certain opinions by expert because he "testified that he has no opinions on them").

If, however, Dr. Sawyer ***is*** seeking to weigh in on general causation (as his

report plainly portends), his claims on that score are not rooted in a reliable methodology for multiple reasons. First, he relies on studies that do not involve valsartan and/or do not involve liver cancer. Second, to the extent he conducts a Bradford Hill analysis, it is incomprehensible, incomplete, and unreliable.

A. Dr. Sawyer Improperly Relies On Animal, Dietary And Occupational Studies, As Well As Studies That Do Not Involve Liver Cancer.

The bulk of Dr. Sawyer's report addresses occupational and dietary studies, many of which do not even involve liver cancer, as well as animal research. Dr. Sawyer's reliance on these inapposite studies is not the product of reliable scientific methods and principles and does not support an admissible opinion on general causation. *See Cohen*, 125 F.4th at 463 ("'there is simply too great an analytical gap between [these studies] and the opinion proffered' by" expert) (citing *Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997)).

Dr. Sawyer's reliance on occupational studies. Like the experts in *Zantac*, Dr. Sawyer relied heavily on work by Mira Hidajat and colleagues on rubber factory workers. (*See, e.g.*, Sawyer Rep. at 4-5, 50, 52, 54, 56, 58, 59, 60-62, 81-82 (citing Mira Hidajat et al., *Lifetime Exposure To Rubber Dusts, Fumes & N-Nitrosamines & Cancer Mortality In A Cohort Of British Rubber Workers With 49 Years Of Follow-Up*, 76 J. Occupational & Env'tl Med. 250 (2019)) ("Hidajat 2019") (Rose Decl. Ex. 8).) As the *Zantac* court recognized, "the number of assumptions and

estimations necessary to render this study helpful to a jury are staggering." *In re Zantac*, 644 F. Supp. 3d at 1215. As an initial matter, "[r]ubber creation leads to the formation of many different types of carcinogens" in the workplace, and working with rubber is a "Group 1"—i.e., known—carcinogen, according to the International Agency for Research on Cancer. *See id.* at 1214. Thus, it is impossible to isolate the effect, if any, of NDMA specifically in that occupational environment.

In addition, routes of exposure matter and "often affect health outcomes[.]" *Id.* at 1216 (citing Fed. Jud. Ctr., *Reference Manual on Scientific Evidence* at 518 (3d ed. 2011)). Rubber workers were exposed through fumes and skin exposure, not through medication taken orally. As a result, for the study to have relevance to the litigation, the testifying expert would have to "testify . . . that the inhaled and absorbed fumes from a 1967 rubber factory may be reliably converted into an ingested dose of" medication. *Id.* at 1216. But, as the *Zantac* court explained, the study author herself has declined to say "whether inhalation or skin absorption of NDMA" at a rubber factory "is analogous to NDMA exposure via oral medication[.]" *Id.* And an expert must not "exceed the limitations the authors themselves place on the study." *Id.* (citation omitted); *see also Cohen*, 125 F.4th at 463 (expert should have been excluded where cited study "cautioned that its 'statistical analyses must be considered preliminary'"). Finally, the study was flawed even on its own terms because "[d]ata on the workers' NDMA exposure" did not

exist, and data on the workers' employment history were sparse. *In re Zantac*, 644 F. Supp. 3d at 1214. In addition, "[w]hether any worker had, after 1967, been exposed to a non-NDMA carcinogen or otherwise had some predilection for cancer was unknown to the researchers." *Id.* In sum, "with assumption piled upon assumption, estimation piled upon estimation . . . the analytical leap from the Hidajat data to the operative inquiry" Dr. Sawyer seeks to answer "is simply too great." *Id.* at 1217.

Dietary studies. Dr. Sawyer also relies on a number of dietary studies, particularly those involving meat. (*See, e.g.*, Sawyer Rep. at 4, 14, 18, 23, 46.) Importantly, as with rubber, meat (especially processed meat) includes a host of potentially toxic or carcinogenic chemicals beyond NDMA, not to mention high levels of fat and (if processed) salt, and is itself a known carcinogen. *In re Zantac*, 644 F. Supp. 3d at 1215. In addition, many of the dietary studies only asked respondents what they had eaten in a particular week, which says nothing about their diets over the course of a lifetime. *Id.* Given these and other limitations, the *Zantac* court identified ***seven*** analytical leaps that an expert had to take to render dietary studies relevant: (1) assuming the accuracy of a subject's memory about what they have eaten; (2) assuming never-changing eating habits (since many of the studies only asked about current dietary habits rather than past or future ones); (3) assuming average NDMA values in food; (4) accounting for other carcinogens in food; (5)

accounting for confounders like smoking; (6) accounting for random chance (given statistically insignificant results); and (7) comparing diet to medication. *Id.* at 1215. Taken together, this is a "leap too far." *Id.*

Reliance on these studies is particularly unreliable given that many of them did not even involve liver cancer, such as Larsson 2006 (gastric cancer), Jakszyn 2012 (prostate cancer), and Jakszyn 2011 (bladder cancer). (*See, e.g.*, Sawyer Rep. at 13-15, 17-19.) As courts have recognized, studies that identify an association between an exposure and one type of cancer cannot be reliably used to reach a causal inference with respect to a different type of cancer. *See, e.g.*, *Magistrini v. One Hour Martinizing Dry Cleaning*, 180 F. Supp. 2d 584, 603 (D.N.J. 2002) ("[I]t is the opinion of this Court that Dr. Ozonoff did not demonstrate a scientifically reliable basis for the inclusion of studies showing an association between PCE and cancers other than leukemia."), *aff'd*, 68 F. App'x 356 (3d Cir. 2003); *Allen v. Pa. Eng'g Corp.*, 102 F.3d 194, 197 (5th Cir. 1996) (while the plaintiff's experts had pointed to evidence "that suggests a connection between EtO exposure and human lymphatic and hematopoietic cancers," such evidence was not "probative on the causation of brain cancer"). The *Zantac* MDL court excluded an expert who "commingled . . . data" from different types of cancer as "depart[ing] from conventional science[.]" *In re Zantac*, 644 F. Supp. 3d at 1233. Dr. Sawyer has done the same here.

Animal models. Finally, Dr. Sawyer also relies heavily on animal research.

(*See, e.g.*, Sawyer Rep. at 9, 10, 14, 80.) As the *Zantac* court explained, animal studies (much like in vitro studies) constitute "secondary evidence" that "cannot *alone* prove general causation," 644 F. Supp. at 1182; rather, at most, they serve "as [a] confirmatory piece[] of the totality of the evidence, *id.* (citation omitted). And even in that limited role, an expert must account for, among other things, "inter-species variability in the bioavailability of NDMA" and "how [to] reliably extrapolate from the dosage of NDMA administered to animals to the dosage consumed by Plaintiffs via" medication. *Id.* at 1280-83. The court rejected the experts' conclusory claims that "humans and animals metabolize NDMA similarly," *id.* at 1281, and concluded that "the analytical gap between the animal data and the causation question is too great," *id.* at 1284. Dr. Sawyer is essentially offering the same boilerplate assertion that "[t]he bioavailability of NDMA, its distribution, metabolism, excretion, and production of highly toxic metabolites is well known and generally accepted in the field of toxicology based on animal experimental studies." (Sawyer Rep. at 80.)

In sum, Dr. Sawyer primarily focuses on occupational, dietary, animal, and non-liver-cancer studies, which cannot even demonstrate an association between exposure to NDMA and the development of liver cancer, let alone causation.

B. Dr. Sawyer's Bradford Hill "Assessment" Is Not The Product Of A Reliable Methodology.

The Bradford Hill framework is a list of nine factors established by Sir Austin

Bradford Hill to help epidemiologists "distinguish a causal connection from a mere association." *In re Zoloft (Sertraline Hydrochloride) Prods. Liab. Litig.*, 858 F.3d 787, 795 (3d Cir. 2017).[17] As courts applying the recently amended Rule 702 have recognized, even though "Bradford Hill is undeniably a reliable methodology . . . the district court ha[s] an independent duty to ensure that all experts 'reliably applied' Bradford Hill." *In re Onglyza*, 93 F.4th at 347; *accord In re Acetaminophen - ASD-ADHD Prods. Liab. Litig.*, MDL No. 3043, 2024 U.S. Dist. LEXIS 121259, at *48 (S.D.N.Y. July 10, 2024) (While "[t]he Bradford Hill analysis has been found to be a 'generally reliable' methodology . . . Rule 702 requires . . . that an expert not only use 'reliable principles and methods' but also that 'the expert's opinion reflects a reliable application of the principles and methods to the facts of the case.'") (quoting Fed. R. Evid. 702).

Importantly, the Bradford Hill criteria only come into play when scientists

[17] These factors are: (1) strength of association (the magnitude of the reported association); (2) consistency of association (whether different studies in different populations consistently report the association); (3) specificity (whether the variable is associated with a specific disease); (4) temporality (whether the exposure precedes disease onset); (5) coherence (whether the causal hypothesis is logical or contradicts existing knowledge); (6) dose-response or biological gradient (whether greater exposure increases risk or vice versa); (7) biological plausibility (whether there is mechanistic evidence of how the agent could cause the disease); (8) experimental evidence (whether experimental studies support the posited association); and (9) analogy (whether the association can reasonably be compared to other associations that have been accepted as causal).

have identified a "perfectly clear-cut" association in the epidemiologic literature. *In re Mirena IUS Levonorgestrel-Related Prods. Liab. Litig. (No. II)*, 341 F. Supp. 3d 213, 265 (S.D.N.Y. 2018), *aff'd*, 982 F.3d 113 (2d Cir. 2020). Given the small body of literature on valsartan and liver cancer, it is unclear how Dr. Sawyer could even perform a proper analysis. And as set forth in Section II.A., above, Dr. Sawyer's heavy reliance on studies that do not involve NDMA in valsartan cannot get him past this threshold question.

Dr. Sawyer nonetheless purports to perform a Bradford Hill "assessment" to support his causality opinion. (Sawyer Rep. at 78-80.) But Dr. Sawyer's three-page discussion of the Hill factors is far too "cursory," "amount[ing] to little more than his ipse dixit." *In re Acetaminophen*, 707 F. Supp. 3d at 357 (excluding expert's "cursory" Bradford Hill discussion, which spanned just a "few pages" and lacked meaningful analysis); *see also In re Valsartan*, 2025 U.S. Dist. LEXIS 66185, at *55 ("Conti's opinion is largely argument and advocacy based on her own *ipse dixit*, rather than a reliable application of economic principles and methods to the facts of the case."). It is also unscientific and results-oriented, further requiring its exclusion.

1. Dr. Sawyer Applies A Shifting And Unreliable Approach To The Strength-Of-Association Criterion.

"[S]trength of the association is the 'cornerstone for causal inferences' because '[t]he higher the relative risk, the stronger the association and the lower the chance that the effect is spurious.'" *In re Paraquat Prods. Liab. Litig.*, 730 F. Supp.

3d 793, 846 (S.D. Ill. 2024) (quoting *Reference Manual on Scientific Evidence* ("*RMSE*") (3d ed. 2011) at 602); *see also Daniels-Feasel v. Forest Pharms., Inc.*, No. 17 CV 4188-LTS-JLC, 2021 WL 4037820, at *8, *16 (S.D.N.Y. Sept. 3, 2021) (strength "is a 'gating' factor"), *aff'd*, 2023 WL 4837521 (2d Cir. July 28, 2023). It is generally accepted that a relative risk under 2.0 (i.e., a doubling of the risk) is facially weak. *In re Viagra (Sildenafil Citrate) & Cialis (Tadalafil) Prods. Liab. Litig.*, 424 F. Supp. 3d 781, 796 (N.D. Cal. 2020) ("[T]he risk factor that emerged across all the studies was somewhere around 1.2," which "undeniably is not a strong association.").

According to Dr. Sawyer, "numerous studies" "leave little or no debate that NDMA is a potent probable human carcinogen that can potentially induce and promote liver cancer." (Sawyer Rep. at 79.) But Dr. Sawyer does not identify what those supposed studies are (*see id.*), rendering his bottom-line assertion inadmissible "*ipse dixit* of the expert." *Joiner*, 522 U.S. at 137. Moreover, when pressed on this sweeping claim at his deposition, Dr. Sawyer conceded that the relative risk reported in the valsartan epidemiology is actually "weak" (Sawyer 5/1/2025 Dep. 111:16-23, 113:13-24)—i.e., in the 1.12 to 1.16 range, far lower than 2.0.[18]

Unable to defend his objectively false characterization of the valsartan

[18] Gomm 2021 (HR 1.16 (95% CI: 1.03-1.31)); Mansouri 2022 (HR 1.12 (95% CI: 1.04-1.22)); Pottegard 2018.

literature in his report, Dr. Sawyer attempted to circumvent the lack of strength at his deposition by arguing that the weak associations are artificially deflated. Essentially, Dr. Sawyer speculates that valsartan studies with longer follow-up periods would show an increased risk ratio at some unknown point in the future. (*See* Sawyer 5/1/2025 Dep. 113:16-24 (opining "that [the risk ratio] number is going to grow at the peak of the latent period, which we don't know what it is yet"); *id.* 114:4-20 ("[I]n the early latency, there's going to be far less -- a lower [risk ratio] than there would be at the peak" and "the peak has not occurred yet. The peak could be at four years . . . ten years. We don't know yet until the studies are carried out longer.").) Dr. Sawyer's speculation regarding "future possibilities" is patently unreliable because courts "must resolve cases on the bas[i]s of scientific knowledge that is currently available[.]" *Phlypo v. BNSF Ry. Co.*, No. 4:17-CV-566-BJ, 2019 WL 2297293, at *8 (N.D. Tex. Mar. 27, 2019) (excluding opinion of expert who "admitted that the scientific community that he cites has not re ached his same conclusions but . . . felt they would possibly reach such a conclusion at some point in the future") (citation omitted). In short, "[l]aw lags behind science; it does not lead it." *In re Mirena*, 341 F. Supp. 3d at 270-71.

Because Dr. Sawyer himself conceded that the relative risks in the relevant studies are weak, his strength opinion is unscientific and cannot support a causal inference.

2. Dr. Sawyer Has No Reliable Basis To Conclude Temporality Is Satisfied.

Epidemiologists must also assess the "temporal relationship of the association—which is the cart and which the horse?"[19] "The question is not whether the exposure precedes the diagnosis but whether it precedes the development of the" disease. *In re Acetaminophen*, 707 F. Supp. 3d at 349. This consideration is not satisfied because Gomm 2021 and Mansouri 2022 assessed individuals just a few years after their use of valsartan, and liver cancer is known to have a long latency period. In other words, many, if not most, of the individuals with cancer in these studies had likely begun to develop liver cancer before they ever took valsartan pills containing NDMA. Dr. Sawyer claims that temporality is nonetheless satisfied because these studies "measured the maximum latency interval at three and five years." (Sawyer Rep. at 80.) But Dr. Sawyer does not set forth any scientific support for the notion that liver cancer has a three-to-five year latency period (and even if true, that would still be far longer than the 23 months during which Mr. Roberts' HCC is alleged to have developed). (*See id.*)[20]

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[19] Hill AB. The Environment and Disease: Association or Causation?. Proc R Soc Med. 1965;58(5):295-300. ("Hill 1965") at 297 (Rose Decl. Ex. 9).

[20] To the extent Dr. Sawyer is offering an opinion that the latency period between Mr. Roberts' first use of valsartan and development of liver cancer was sufficient for causation (*see* Sawyer Rep. at 80), he is not qualified to offer that opinion because: he is not a physician, let alone a hepatologist; his opinion is pure *ipse dixit* since he does not identify the date on which Mr. Roberts was exposed to

Dr. Sawyer's temporality opinion is also fundamentally inconsistent with his prior reliance in other litigation on CDC guidance, which identifies a 4-year latency for solid cancers and relies on a study showing a ***12-year*** latency period for liver cancer.[21] (*See* Sawyer 5/1/2025 Dep. 84:11-18, 85:8-23.) It is also at odds with Dr. Sawyer's treatment of cancer latency in the glyphosate litigation, where he cited a paper that referenced a 10.8 year liver cancer latency period.[22] In short, Dr. Sawyer's shifting approach to latency is not just conclusory; it is inherently results-driven.

Dr. Sawyer also suggests, based on animal studies, that the "promotor abilities of NDMA" can induce a shortened latency period for liver cancer. (Sawyer Rep. at

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enough NDMA in valsartan to supposedly cause liver cancer or explain why the latency period from that date until Mr. Roberts' diagnosis sufficed; and he offers no basis to conclude that Mr. Roberts' liver cancer developed after he began using valsartan.

[21] *See* Expert Report of Dr. William Sawyer dated June 24, 2021, *Vosper, et al. v. Monsanto*, at 179 (Rose Decl. Ex. 10) (citing a World Trade Center Health Program guidance document to estimate the latency period for non-Hodgkin lymphoma from glyphosate exposure); World Trade Ctr. Health Program, "*Minimum Latency & Types or Categories of Cancer*" (John Howard, Administrator, Oct. 17, 2021, rev. Jan 6, 2015, *available at* https://www.cdc.gov/wtc/pdfs/policies/WTCHP-Minimum-Cancer-Latency-PP-01062015-508.pdf) at 5 ("The minimum latency of 12 years has been reported for liver cancer associated with vinyl chloride exposure (Lelbach 1996).") (Rose Decl. Ex. 11).

[22] *See* Expert Report of Dr. William Sawyer dated June 24, 2021, *Vosper, et al. v. Monsanto*, at 179 (citing Nadler and Zurbenko 2013 (Rose Decl. Ex. 10) for his glyphosate and non-Hodgkin lymphoma latency estimate); Nadler, Diana L. et al., Developing a Weibull Model Extension to Estimate Cancer Latency. International Scholarly Research Notices. 2013; 750857 ("Nadler 2013") at 75-76 (Rose Decl. Ex. 12).

80.) But, as he admitted, the only citation he provided to support such an opinion was an "error." (Sawyer 5/1/2025 Dep. 99:17-23.) Dr. Sawyer could not identify any actual scientific research (human or animal) demonstrating that NDMA accelerates the growth of already-existing cancers.

For this reason, too, his Bradford Hill analysis was unreliable.

3. Dr. Sawyer's Dose-Response Conclusion Contradicts Scientific Consensus.

The dose-response factor assesses whether "a change in amount, intensity, or duration of exposure to an agent is associated with a change—either an increase or decrease—in risk of disease." *McClain v. Metabolife Int'l, Inc.*, 401 F.3d 1233, 1241-42 (11th Cir. 2005) (citation omitted). In his report, Dr. Sawyer claims that "[m]any of the studies revealed statistically significant dose-response effects, some of which were linear" (Sawyer Rep. at 79), but that is simply not true. Pottegard 2018 expressly found no evidence of dose-response.[23] Gomm 2021 similarly found that "[l]ong-term use showed no association with the change in overall cancer rate."[24] And Mansouri 2022 reported an ***inverse*** relationship between increased use of valsartan with NDMA and risk of cancer.[25] As such, Dr. Sawyer's dose-response opinion amounts to claiming that a dose-response exists even though "no study [has]

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23 Pottegard 2018 at 1.

24 Gomm 2021 at 358.

25 Mansouri 2022 at 9.

concluded such a relationship existed, with some even observing the inverse of a dose-response relationship." *In re Zantac*, 644 F. Supp. 3d 1240 (excluding expert for taking a similar approach to dose-response).

When confronted with these studies at his deposition, Dr. Sawyer conceded that they all found no evidence of a dose-response relationship, confirming that his opinion on this critical Hill factor is scientifically unsupportable. (*See* Sawyer 5/1/2025 Dep. 147:13-17, 148:2-25.) At his deposition, Dr. Sawyer nonetheless purported to identify evidence of a dose-response relationship "[b]ased upon the human dietary studies as well as the occupational Hidajat study" (*id.* 149:5-7), going as far as to claim that the dietary and occupational studies are better than the valsartan studies because of the "robust database" and "size of the dose response data" included in those studies (*id.* 122:1-4, 128:1-3). But as explained in detail above, "there are too many inherent uncertainties in the dietary epidemiology and the [Hidajat 2019] occupational study for such data to be reliably applied to the causation question[.]" *In re Zantac*, 644 F. Supp. 3d at 1215, 1217. This is particularly true for the dose-response question because the only dietary study to assess NDMA exposure and liver cancer found no dose-response relationship either. Indeed, the authors reported a lower odds ratio for the greatest intake of NDMA from dietary sources compared to the smallest intake of NDMA from dietary sources.[26] In

[26] Zheng J. Daniel CR, et at., Dietary N-Nitroso Compounds and Risk of

short, Dr. Sawyer effectively conceded that his approach to dose-response is not rooted in the valsartan literature and instead relies on inapposite occupational and dietary studies that the *Zantac* court appropriately recognized do not provide good grounds for a general causation opinion.

4. Dr. Sawyer Applies An Unreliable Methodology To Conclude That The Epidemiology Is Consistent.

Consistency of association—whether the observed association has "been repeatedly observed by different persons, in different places, circumstances and times"[27]—is important because "[d]ifferent studies that examine the same exposure-disease relationship generally should yield similar results." *RMSE* at 604. Here, two studies found small statistically-significant associations between the use of valsartan containing NDMA and liver cancer, whereas the third valsartan study reported no statistically significantly increased risk. Further, the authors of all three studies uniformly disclaimed any findings of causality.[28] *See In re Zantac*, 644 F. Supp. 3d

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Hepatocellular Carcinoma: A USA-Based Study. Hepatology. 2021;74(6):3161-3173 ("Zheng 2021") at Table 2 (Rose Decl. Ex. 13). Dr. Sawyer also recognized that the authors reported no significant p-trend, a statistical tool to test whether there is a dose-response. (*See* Sawyer 5/1/2025 Dep. 156:20-157:5.)

[27] Hill 1965 at 296.

[28] *See* Pottegard 2018 at 6 ("findings suggest that the levels of NDMA exposure achieved through valsartan products do not translate into a substantially increased short term cancer risk"); Gomm 2021 at 360 ("[c]ausality cannot be inferred"); *see also* Mansouri 2022 at 12 ("[m]ore research is needed to gain further evidence and to understand more deeply the relationship between NDMA exposure and the risks of liver cancer").

at 1234 (excluding expert opinions on the basis that they "have no independent, epidemiological scientific support for their conclusions" where "[a]lmost every scientific study authored . . . has concluded that there is no evidence of an association between ranitidine and cancer" and "[e]ven the studies that facially found some evidence of an association exercised great restraint and caution in their conclusions, a far cry from any conclusion that ranitidine causes cancer").[29]

Presumably because one-third of the relevant valsartan epidemiological studies found no statistically significant increased risk of liver cancer, and all disclaim causality, Dr. Sawyer discounted that body of evidence at his deposition and focused instead on dietary and occupational rubber studies as establishing consistency.[30] (*See, e.g.*, Sawyer 5/1/2025 Dep. 144:13-18 (opining "there was consistency found in [the NDMA dietary] studies"); *id.* 130:15-16 (stating that for the consistency factor, "there are other studies that [he] relied on both, dietary and occupational").) But even if it were proper to rely on dietary and rubber factory studies to manufacture consistency of association, Dr. Sawyer's analysis would not

[29] As set forth in detail above, the single citation Dr. Sawyer includes as support for his ultimate conclusion that there is consistency of association among the valsartan studies, dietary studies and occupational cohorts is a falsified citation. This alone warrants exclusion of his consistency opinion and demonstrates the unreliable and ad hoc approach Dr. Sawyer took to formulating his general causation opinion.

[30] Dr. Sawyer backed away from the valsartan studies despite admitting that they were "important" because they examined "real world exposure" of "the actual drug itself with the contaminant in it." (Sawyer 5/1/2025 Dep. 120:7-18.)

be reliable.

First, of the 15 studies cited by Dr. Sawyer that examined the alleged association between NDMA and diet, only one (Zheng 2021) actually examined liver cancer. (Sawyer 5/1/2025 Dep. 151:7-18.) Dr. Sawyer's reliance on studies that did not investigate the alleged association between NDMA and the cancer at issue in this litigation renders his methodology unreliable. *See, e.g.*, *Hoefling v. U.S. Smokeless Tobacco Co., LLC*, 576 F. Supp. 3d 262, 272-73 (E.D. Pa. 2021) (excluding expert whose sources "found a causative link only to oral-cavity, esophageal and pancreatic cancer" but not to the oropharyngeal cancer at issue because "[p]atients are not diagnosed with 'head and neck cancer' but rather cancers of more narrowly defined anatomical sites, which have different risks"); *Jones v. Novartis Pharms. Corp.*, 235 F. Supp. 3d 1244, 1269-72 (N.D. Ala. 2017) (excluding expert because he had "not first established that there is an association between Reclast [the drug at issue] and AFFs [the injury at issue]"); *In re Zantac*, 644 F. Supp. 3d at 1233 (noting expert's practice of combining data related to various different cancers "depart[ed] from conventional science" and rendered her opinion unreliable). Even Dr. Sawyer conceded that "if liver was not an organ that was tested in the study, yes, I would give very little weight." (Sawyer 5/1/2025 Dep. 58:20-59:2.)

In any event, even if the dietary studies were relevant, Dr. Sawyer further conceded that their results were "quite variable" (*id.* 144:13-18; *see also* Sawyer

Rep. at 79 ("[d]ietary studies were less consistent"))—i.e., not consistent. For example, in the single study that investigated the association between dietary NDMA intake and liver cancer, there was no reported association between NDMA consumption from animal and plant sources and liver cancer, but an association was detected for NDMA from plant sources only.[31] Such "conflicting data . . . signify[] an inherent problem with the study design's accuracy of exposure" and presumably for this reason, the study authors concluded that "'NDMA . . . effects . . . warrant further prospective investigation.'" *In re Zantac*, 644 F. Supp. 3d at 1212 (citation omitted).

Second, Dr. Sawyer claims that Hijadat 2019—a single epidemiology study—demonstrates consistency. (Sawyer 5/1/2025 Dep. 144:25-145:3 ("Q. But you said that the dietary studies had less consistency than Hidajat . . . Hidajat is a single study. Right? A. Yes."); Sawyer Rep. at 79 ("There is reasonable consistency of liver cancer, especially in the valsartan and occupational studies of industrial rubber production industry workers.").) But "[a] single study of a single incident is by definition insufficient to establish consistency." *In re Flint Water Cases*, No. 16-10444, 2024 WL 21786, at *5 (E.D. Mich. Jan. 2, 2024). And while Dr. Sawyer originally testified that he considered other rubber industry studies in his consistency

[31] *See* Zheng 2021. (*See also* Sawyer Rep. at 32.)

analysis (Sawyer 5/1/2025 Dep. 136:20-137:13), he changed his tune when he realized those studies did not identify an association with liver cancer and did not contain "NDMA specific data" (*id.* 141:20-24).

In sum, Dr. Sawyer seeks to manufacture consistency by disregarding the most relevant epidemiologic studies and instead relying on select NDMA studies that are, in any event, themselves inconsistent. This is the hallmark of an unreliable approach to consistency.

5. Dr. Sawyer Applies An Unreliable Methodology For The Remaining Bradford Hill Factors As Well.

Dr. Sawyer's opinions regarding the remaining Bradford Hill factors—biological plausibility, specificity, coherence, analogy, and experiment—are similarly unreliable and unscientific.

Biological Plausibility. "While *Daubert* does not require absolute precision in identifying the medical mechanism of injury, there still must be 'sufficiently compelling proof'" of that mechanism. *Soldo v. Sandoz Pharms. Corp.*, 244 F. Supp. 2d 434, 561-62 (W.D. Pa. 2003) (citation omitted). Dr. Sawyer claims that the "mechanisms of induction and promotion of liver cancer by NDMA" have been "thoroughly assessed" in his report (Sawyer Rep. at 79), but as set forth above, his opinions regarding potential mechanisms by which NDMA can cause liver cancer (*see generally id.* at 6) contain numerous falsified citations. Dr. Sawyer therefore has no reliable basis to provide these opinions. Dr. Sawyer also asserts that

"[n]umerous animal studies" provide "a reasonable under-standing of the actual mechanisms" (*id.* at 80), but animal studies are not admissible to prove human causation absent "good grounds to extrapolate from animals to humans," *In re Human Tissue Prods. Liab. Litig.*, 582 F. Supp. 2d 644, 657 (D.N.J. 2008) (quoting *In re Paoli R.R. Yard PCB Litig.*, 35 F.3d 717, 743 (3d Cir. 1994)); *Soldo*, 244 F. Supp. 2d at 548 (excluding testimony because "plaintiff's experts did not demonstrate that . . . the species in which these studies were performed[] were sufficiently similar to . . . human being[s]"), which has plainly not been demonstrated in this case.

Specificity. "Specificity, in laymen's terms generally means that an agent usually causes one type of human [disease]. When an agent is associated with a broad array of different types of diseases it weakens the evidence because it is non-specific." *Gannon v. United States*, 571 F. Supp. 2d 615, 626 (E.D. Pa. 2007), *aff'd*, 292 F. App'x 170 (3d Cir. 2008). It is unclear whether Dr. Sawyer deems specificity satisfied because he merely states that "NDMA has been shown to have multiple carcinogenic endpoints" (Sawyer Rep. at 79)—i.e., NDMA has not been linked specifically with liver cancer. And specificity of association cannot be glossed over because its absence "highlights the complexity of the causation analysis." *In re Acetaminophen*, 707 F. Supp. 3d at 349 (excluding opinion that specificity "factor is considered to be 'all but irrelevant' by modern epidemiologists").

Coherence. Coherence means that "the cause-and-effect interpretation of our data should not seriously conflict with the generally known facts of the natural history and biology of the disease."[32] Dr. Sawyer's coherence opinion ignores numerous anomalies in the NDMA-valsartan epidemiology that render Dr. Sawyer's causation opinion incoherent with scientific knowledge. For example, although Gomm 2021 identified "a slight elevation in the risk of liver cancer with the use of potentially NDMA-contaminated valsartan," the 3-year long-term use data showed no statistically significant association with liver cancer.[33] And in Mansouri 2022, the "slight increased risk of liver cancer . . . in patients exposed to NDMA in regularly taken medications" was isolated to men and the poorest 20%, with a protective effect identified from use of valsartan containing NDMA and liver cancer in women and the remaining social deprivation indexes demonstrating non-statistically significant figures.[34] It is incoherent for studies to provide differing risk ratios on the basis of length of use, gender and social class.

Analogy. Analogy refers to comparing an agent known to cause a specific disease to another, similar agent.[35] Dr. Sawyer seeks to analogize NDMA to NDEA,

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32 Hill 1965 at 298.

33 Gomm 2021 at 358 (HR 1.22 (95% CI: 0.80-1.89) for long-term use).

34 Mansouri 2022 at 10 fig. 3 (HR 0.90 (95% CI: 0.75-1.07) for women), 12.

35 Hill 1965 at 299.

but there are no studies linking NDEA to liver cancer in humans.[36] (Sawyer Rep. at 80 ("Analogy is evident" because "NDMA's close cousin, NDEA, is structurally similar to NDMA with similar toxic metabolites . . . that also produce similar malignancies. . . ").) Such a conclusory "analogy" opinion—which amounts to basically no opinion at all—is unreliable and inadmissible. *See In re Acetaminophen*, 707 F. Supp. 3d at 351 (excluding proffered analogy of acetaminophen to valproic acid as a "bare assertion, unaccompanied by any discussion").

Experiment. Hill also asks whether a causal relationship is supported by "experimental, or semi-experimental, evidence."[37] Dr. Sawyer relies on animal evidence to support his causal theory, but the animal studies have not—and cannot—reliably be extrapolated to form a causal connection in humans.[38] *See In re Acetaminophen*, 707 F. Supp. 3d at 358 (excluding opinion that experiment factor satisfied based on expert's "highly inaccurate representation of the animal study

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[36] At the March 2, 2022 *Daubert* hearing, Judge Kugler precluded Dr. Panigrahy, plaintiffs' general causation epidemiologist, from "express[ing] an opinion as to NDEA exposure" and liver cancer because of the lack of supportive evidence. (*See* ECF No. 1959, at 153:12-19; *see also Daubert* Hearing Order at 1, ECF No. 1958, at 2 (excluding Dr. Panigrahy's opinions on NDEA exposure and liver cancer).)

[37] Hill 1965 at 298.

[38] (*See, e.g.*, Chodosh Sec. Supp. Rep. ¶ 38 (Rose Decl. Ex. 14) (explaining that "the notion that NDMA causes cancer at doses that are orders of magnitude lower than the lowest dose observed to cause cancer in experimental animals makes [Dr. Sawyer's causation] theory decidedly implausible").)

literature").

In short, Dr. Sawyer's Bradford Hill analysis is unreliable, conclusory, and result-oriented at every step. As such, he should not be allowed to offer any testimony about causation at trial.

III. DR. SAWYER'S DOSE EXTRAPOLATION CALCULATIONS ARE UNRELIABLE.

Dr. Sawyer also seeks to opine that "Mr. Roberts' ingested oral dosage of NDMA" in valsartan for less than two years "statistically and significantly increased his risk of liver cancer" based on: (1) his purported conversion of the dose of NDMA inhaled by rubber factory workers in Hidajat 2019 into a "systemic dose" that would have been absorbed into the workers' bodies; (2) comparing that "systemic" dose to the "systemic" dose of NDMA orally ingested by Mr. Roberts; and (3) using that comparison to apply the risk estimates observed in Hidajat 2019 to Mr. Roberts. (Sawyer Rep. at 81-82.) In other words, Dr. Sawyer attempts to make the risk estimates in Hidajat 2019 relevant to this case by developing a "route-to-route" method that purportedly converts the occupational inhalation exposures in Hidajat 2019 to Mr. Roberts' ingestion of valsartan.

The *Zantac* court previewed that such a conversion calculation would be unreliable given the many limitations of Hidajat 2019 discussed above. According to the *Zantac* court, "[f]or the Hidajat study to possess some level of relevance, an expert would have to testify at trial that the inhaled and absorbed fumes from a 1967

rubber factory may be reliably converted into an ingested dose of" medication containing NDMA. 644 F. Supp. 3d at 1216-17. The court made clear, however that "such a conclusion would . . . 'exceed the limitations the authors themselves place on the study,' as the Hidajat study was clearly meant to address the risks of exposure from an occupation, rubber creation." *Id*. Further, the court explained that "for such a conversion to be part of a reliable methodology, it would also have to be weighed in conjunction with assumptions about how long a worker worked, where they worked, and what they were exposed to," since this information was not available to the authors of the studies. *Id*. at 1217. According to the *Zantac* court, such a route-to-route conversion analysis would be based on "assumption piled upon assumption, estimation piled upon estimation," making the "the analytical leap from the Hidajat data to" conclusions regarding causation in a case involving a pharmaceutical product "simply too great." *Id*.

Dr. Sawyer's opinions are unreliable for the same reasons.

First, Dr. Sawyer himself acknowledges that his route-to-route extrapolation method has not been peer-reviewed or published in its entirety in any scientific source, claiming that it is "too basic" to publish. (Sawyer 5/2/2025 Dep. 19:16-20:10; *see also id.* 17:6-18; 18:6-22.) But this *ipse dixit* assertion, unsupported by any scientific evidence, is not sufficient to demonstrate that Dr. Sawyer's "methodology has widespread or general acceptance in the scientific community"

and therefore it does not satisfy Rule 702. *See In re Zantac*, 644 F. Supp. 3d at 1270 (excluding cumulative exposure calculations where expert could not establish his method was a "generally accepted methodology"); *see also Valsartan*, 2025 U.S. Dist. LEXIS 66185, at *53-54 ("Plaintiffs rely solely on Conti's *ipse dixit* and speculation, rather than scientific principles.").

Second, as the *Zantac* court expressly recognized, the Hidajat 2019 study suffers from a "staggering" "number of assumptions and estimations" regarding the exposures of the factory workers studied that make it impossible to reliably calculate those workers' NDMA inhalation doses, much less convert them to a systemic dose. 644 F. Supp. 3d at 1215. As noted above, the Hidajat 2019 authors did not have data regarding the studied workers' NDMA exposure. *Id*. at 1214. Thus, the authors had to ***estimate*** the workers' NDMA exposures based on the job duties and location of work in ***other*** rubber factories in other countries. But the risk estimates were premised on a number of speculative assumptions, including that:

- The workers continued to work in the factory after 1967, the only year for which the Hidajat 2019 authors had employment data;
- The workers stayed in the same departments with the same NDMA exposure levels for the rest of their careers;
- Each worker retired at 70 years of age;
- No worker ceased to work at any point prior to 70; and
- The workers never left the rubber industry to be exposed to different carcinogens in some other occupation.

See id. The reliability of the exposure estimates in Hidajat 2019 is even more questionable because 90% of the NDMA measurements employed by the authors were below the detection limit, meaning that the authors simply guessed as to how much actual NDMA was in the air in the various rubber factories. (*See* Sawyer 5/2/2025 Dep. 88:9-19, 92:6-10.) Given these "assumptions, estimations, [and] potential for confounding," even experts for the plaintiff in *Zantac* conceded, and the court agreed, that "the dose and length of exposure may not have been accurately ascertained if at all" in Hidajat 2019. *In re Zantac*, 644 F. Supp. 3d at 1216. These same assumptions significantly undermine the reliability of Dr. Sawyer's calculations based on the Hidajat 2019 exposure estimates.

Fourth, Hidajat 2019 did not account for the fact that workers were simultaneously exposed to dozens of chemicals in the occupational setting (as opposed to NDMA alone), or for other potential confounders that could have affected liver cancer risks. Exposure to potentially carcinogenic substances in rubber factories is so prevalent that employment in the rubber industry itself is considered "carcinogenic to humans" by IARC.[39] Notably, Hidajat 2019 did not have any information about, and could not control for, "[w]hether any worker had, after 1967, been exposed to a non-NDMA carcinogen," either in the factory or in some other

[39] IARC, Chemical Agents and Related Occupations, Vol. 100, at 559 (2012) (Rose Decl. Ex. 15).

manner. *In re Zantac*, 644 F. Supp. 3d at 1214. The authors also did not consider whether the workers "had some predilection for cancer [that] was unknown to the researchers" that could have affected liver cancer risk, such as smoking or alcohol use. *Id.* For this reason too, Dr. Sawyer's exposure assessment seeks to extrapolate from data that is itself patently unreliable and therefore his calculations are not based on a reliable method. *See, e.g., Kilpatrick v. Breg, Inc.*, 613 F.3d 1329, 1341 (11th Cir. 2010) (affirming the exclusion of an expert because the "speculative" literature that the expert "based his conclusions upon was insufficient to create a reliable methodology which passes *Daubert* muster"); *In re Viagra Prods. Liab. Litig.*, 658 F. Supp. 2d 936, 945 (D. Minn. 2009) (excluding an expert on the basis that his methodology was unreliable because "to the extent that it is based on the McGwin [s]tudy as published, [it] lacks sufficient indicia of reliability to be admitted as a general causation opinion").

CONCLUSION

For the reasons set forth above, the Court should exclude Dr. Sawyer's opinions.

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Respectfully submitted,

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CERTIFICATE OF SERVICE

I HEREBY CERTIFY that on May 22, 2025, a true and correct copy of the foregoing document was served upon counsel of record via operation of the Court's electronic filing system.

Dated: May 22, 2025

Respectfully submitted,

/s/ Jessica Davidson

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